

**In the Claims:**

In response to the Office Action dated June 3, 2003 (Paper No. 16), finally rejecting claims 1, 2, 4, 8, 11, 16 and 17, please amend the above-identified U.S. patent application as follows:

Claim 1 (cancelled)

Claim 2 (currently amended): A fusion protein comprising human alpha 1-antitrypsin or a functionally active portion thereof, and human secretory leukocyte protease inhibitor or a functionally active portion thereof, wherein said fusion protein has protease inhibitor activity.

Claim 3 (withdrawn): A fusion protein comprising alpha 1-antitrypsin or a functionally active portion thereof, and a tissue inhibitor of metalloproteases or a functionally active portion thereof, wherein said fusion protein has protease inhibitor activity.

Claim 4 (currently amended): The fusion protein of claim 2, comprising

- a) amino acids from about 1 to about 394 of human alpha 1-antitrypsin; and
- b) amino acids from about 1 to about 107 of human secretory leukocyte protease inhibitor.

Claim 5 (withdrawn): A polynucleotide encoding the fusion protein of claim 1, 2, 3, or 4.

Claim 6 (withdrawn): An expression vector comprising the polynucleotide of claim 5.

Claim 7 (withdrawn): A host cell comprising the expression vector of claim 6.

Claim 8 (currently amended): A pharmaceutical composition comprising the fusion protein of claim [[1,]] 2, 3, or 4 admixed with a pharmaceutically acceptable vehicle.

Claim 9 (withdrawn): A method of producing the fusion protein of claim 1, 2, 3, or 4, said method comprising culturing a transformed host cell containing an expression vector encoding a fusion protein under conditions appropriate for expressing said fusion protein.

Claim 10 (withdrawn): The method of claim 9 further comprising purifying said fusion protein.

Claim 11 (cancelled)

Claim 12 (withdrawn): The fusion protein of claim 1, wherein the second protease inhibitor inhibits a metalloprotease.

Claim 13 (withdrawn): The fusion protein of claim 1 wherein the second protease inhibitor inhibits an aspartyl protease.

Claim 14 (withdrawn): The fusion protein of claim 1 wherein the second protease inhibitor inhibits a cysteine protease.

Claim 15 (withdrawn): The fusion protein of claim 3 wherein the tissue inhibitor of metalloproteases is TIMP-1 or a functionally active portion thereof.

Claim 16 (original): The fusion protein of claim 4 wherein the carboxy terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin is linked to the amino terminus of amino acids from about 1 to about 107 of secretory leukocyte protease inhibitor.

Claim 17 (original): The fusion protein of claim 4 wherein the carboxy terminus of amino acids from about 1 to about 107 of secretory leukocyte protease inhibitor is linked to the amino terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin.

Claim 18 (withdrawn): The fusion protein of claim 3, comprising

- a) amino acids from about 1 to about 394 of alpha 1-antitrypsin; and
- b) amino acids from about 1 to about 184 of tissue inhibitor of metalloproteases-1.

Claim 19 (withdrawn): The fusion protein of claim 18 wherein the carboxy terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin is linked to the amino terminus of amino acids from about 1 to about 184 of tissue inhibitor of metalloproteases-1.

Claim 20 (withdrawn): The fusion protein of claim 18 wherein the carboxy terminus of amino acids from about 1 to about 184 of tissue inhibitor of metalloproteases-1 is linked to the amino terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin.

Claim 21 (withdrawn): The fusion protein of claim 3 comprising

a) amino acids from about 1 to about 394 of alpha 1-antitrypsin; and

b) amino acids from about 1 to about 126 of tissue inhibitor of metalloproteases-1.

Claim 22 (withdrawn): The fusion protein of claim 21 wherein the carboxy terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin is linked to the amino terminus of amino acids from about 1 to about 126 of tissue inhibitor of metalloproteases-1.

Claim 23 (withdrawn): The fusion protein of claim 21 wherein the carboxy terminus of amino acids from about 1 to about 126 of tissue inhibitor of metalloproteases-1 is linked to the amino terminus of amino acids from about 1 to about 394 of alpha 1-antitrypsin.

Claim 24 (withdrawn): A fusion protein comprising

a) a polypeptide comprising amino acids from about 1 to about 394 of alpha 1-antitrypsin; and

b) a polypeptide comprising amino acids from about 1 to 127 of tissue inhibitor of metalloproteases-1, wherein the alpha 1-antitrypsin polypeptide is covalently linked to the tissue inhibitor of metalloproteases-1 polypeptide through a disulfide bond between amino acid 127 of the tissue inhibitor of metalloproteases-1 polypeptide and a free cysteine residue of the alpha 1-antitrypsin polypeptide,

wherein said fusion protein has protease inhibitor activity.

Claim 25 (withdrawn): The fusion protein of claim 24 wherein the free cysteine residue of the alpha 1-antitrypsin polypeptide is at position 232 in SEQ ID NO: 2.

Claim 26 (withdrawn): A method for inhibiting protease activity, comprising contacting the protease with the fusion protein of claims 1, 2, 3, or 4.

Claim 27 (withdrawn): The method of claim 26 wherein the protease activity is associated with a disorder selected from the group consisting of emphysema, asthma, chronic obstructive pulmonary disease, cystic fibrosis, otitis media, and otitis externa.

Claim 28 (withdrawn): The method of claim 26, wherein the protease activity is associated with HIV infection.

Claim 29 (withdrawn): The method of claim 26, wherein the fusion protein is contacted with the protease by administering the fusion protein to an individual having the protease.

Claim 30 (withdrawn): A method of treating an individual suffering from, or at risk for, a disease or disorder involving unwanted protease activity comprising administering to the individual an effective amount of the fusion protein of claims 1, 2, 3, or 4.

Claim 31 (withdrawn): The method of claim 30, wherein the individual suffers from emphysema.

Claim 32 (withdrawn): The method of claim 30, wherein the individual suffers from asthma.

Claim 33 (withdrawn): The method of claim 30, wherein the individual suffers from chronic obstructive pulmonary disease.

Claim 34 (withdrawn): The method of claim 30, wherein the individual suffers from cystic fibrosis.

Claim 35 (withdrawn): The method of claim 30, wherein the individual suffers from otitis media or otitis externa.

Claim 36 (new):       The fusion protein of claim 4, comprising SEQ ID NO: 8.

Claim 37 (new):       The fusion protein of claim 4, comprising SEQ ID NO: 16.